

Prior Art Rejections

Rejection under 35 U.S.C. § 103(a) over Chu (U.S. 6,284,194) in view of Nanbu et al. (U.S. 6,130,055) or Uenoyama et al. (U.S. 5,856,117)

The rejection of claims 5, 12, 27, 31, 41, 45, 53 and 60 under 35 U.S.C. § 103(a) as being unpatentable over Chu (U.S. 6,284,194) in view of Nanbu et al. (U.S. 6,130,055) or Uenoyama et al. (U.S. 5,856,117) is respectfully traversed.

The Position of the Examiner

It is the position of the Examiner that Chu discloses an analytical device and a method of making the device, wherein the device comprises a porous reaction membrane and at least one receptor immobilized in a limited region. The Examiner states that Chu teaches applying a surfactant (surface active agent) to the reaction membrane and allowing it to dry. The Examiner further states that Chu teaches the surfactant can be polyoxyethylene (23), polyoxyethylene sorbitan monolaurate or polyoxyethylene sorbitan monooleate. The Examiner admits that Chu fails to teach a surface active agent comprising sugar in a hydrophilic part of the surface active agent.

The Examiner asserts that Nanbu et al. and Uenoyama et al. disclose surfactants used in bioassays, and that surfactants improve assay sensitivity. The Examiner further states that Nanbu et al. and Uenoyama et al. teach the equivalence of polyoxyethylene sorbitan monolaurate and polyoxyethylene sorbitan monooleate to sucrose monolaurate surfactants (Nanbu et al.) and n-octyl-B-D-thioglucoside (Uenoyama et al.).

Therefore, the Examiner takes the position that it would have been obvious to substitute the surfactants of Nanbu et al. or Uenoyama et al. for the surfactant of Chu, because the references teach that surfactants improve assay sensitivity, and because the references show equivalence among the surfactants.

Object and Advantages of Applicants' Claimed Invention

Applicants' claim 5 recites a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized, wherein the reactive layer includes a surface active agent that is solidified when dried, and wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

Applicants' claim 12 recites a method for manufacturing a chromatography medium which comprises a reactive layer on which at least one reactive component for a chromatographic analysis is immobilized comprising: (a) impregnating or coating the reactive layer of the chromatography medium with a liquid, wherein a surface active agent which is solidified when dried is dissolved in the liquid; and (b) drying the reactive layer which has been impregnated or coated with the liquid in which the surface active agent is dissolved, wherein the surface active agent comprises a sugar in a hydrophilic part of the surface active agent.

Applicants' invention results in reduced influences on the specific protein which is immobilized to the reaction layer, as well as reduced denaturation or deactivation of the specific protein. Therefore, a chromatography medium with enhanced reactivity is achieved, due to enhanced permeation of the reactive layer and uniform permeation of a sample, thus resulting in a chromatography measurement with a higher sensitivity and higher performance.

Additionally, by employing a surface active agent that is solidified when dried, the devitalization of the specific protein immobilized to the reactive layer can be minimized, thus realizing enhanced preservation stability of the chromatography specimen, extended quality maintenance period and expanded storage condition of the chromatography medium. (See page 7, lines 14-19 of the disclosure.)

Further, by using a surface active agent which comprises sugar in a hydrophilic part, in addition to the advantages discussed above, the solubility is enhanced and the permeability is increased by the action of the sugar. Additionally, influence on the reactive component (specific protein) can be reduced, and the denaturization and

devitalization of the immobilized protein can be minimized, resulting in a reactive layer which can perform for a long time. (See page 9, lines 1-11 of the disclosure.)

Applicants' Arguments

The primary reference cited by the Examiner (Chu) belongs to a technical field that is similar to the technical field of Applicants' presently claimed invention; and has a similar construction to Applicants' presently claimed invention. Although Chu discloses more than 30 kinds of surfactants, as admitted by the Examiner, Chu fails to teach or suggest a surfactant which satisfies Applicants' claims. [Applicants note that the present specification discusses a document which is similar to the Chu reference, i.e., the discussed document teaches the same surfactants as taught in the Chu reference.]

The Examiner has turned to two secondary references (Nanbu et al. and Uenoyama et al.) in an attempt to "find" a surfactant which may meet Applicants' claimed requirements.

The Nanbu et al. reference relates to a method for measuring trypsin-inhibitor (UTI) included in urine. Nanbu et al. disclose that activity of a proteolytic enzyme is improved by containing a surfactant. On the other hand, Applicants' invention has no relation to the proteolytic enzyme. Further, Nanbu et al. disclose that the surfactant has no limitation in kind, and may be an ionic surfactant, an amphoteric surfactant, or a nonionic surfactant. Nanbu et al. do not place any criticality on the specific surfactant employed. Thus, many known surfactants are broadly disclosed by the Nanbu et al. reference. However, the Examiner fails to discuss, or even mention, most of the surfactants disclosed by the reference. Instead, the Examiner has picked and chosen from among the broad teachings of Nanbu et al., and has chosen to look only to a surfactant including sugar, in an attempt to satisfy Applicants' claims. However, the Examiner has provided no reason why one of ordinary skill in the art, reading the disclosure of Nanbu et al., would make this very specific choice.

Uenoyama et al. disclose a reaction system for measuring the concentration of urinary trypsin inhibitors comprising mixing a urine sample, a protease solution containing trypsin, and a buffer solution, adding a substrate and measuring the activity of

an enzyme. Further, Uenoyama et al. provide a reaction system in which the dissolubility of a poorly-water soluble substrate is improved by using a surfactant. This invention is unrelated to Applicants' invention.

Uenoyama et al. disclose 16 kinds of surfactants as an amphoteric surfactant or a nonionic surfactant. However, only two surfactants of those taught by Uenoyama et al. are applicable to Applicants' invention. Thus, the remaining fourteen surfactants are inapplicable to Applicants' invention. However, the Examiner does not mention any of the non-applicable surfactants disclosed by the reference. Instead, similar to the discussion regarding Nanbu et al., the Examiner has picked and chosen from among the broad teachings of Uenoyama et al., and has chosen to look only to a surfactant including sugar, in an attempt to satisfy Applicants' claims. However, the Examiner has provided no reason why one of ordinary skill in the art, reading the disclosure of Uenoyama et al., would make this very specific choice.

The Examiner states that the secondary references have been relied upon for teaching that the use of surfactants with sugar in a hydrophilic part is known. However, merely establishing that these surfactants are known in the art does not establish a *prima facie* case of obviousness. It appears that the Examiner is attempting to employ an "obvious to try" rationale, i.e. to try the various surfactants of Nanbu et al. and Uenoyama et al. in the composition of Chu. However, Applicants respectfully assert that the "attempted" rationale employed by the Examiner in rejecting Applicants' claims was recently addressed by the Supreme Court in KSR International Co. v. Teleflex Inc., 127 S.Ct. 1727 (U.S. 2007). The Examiner's rejection does not articulate the requirements necessary to reject the claims based on this rationale.

Discussion Regarding KSR Decision

In KSR, the Supreme Court addressed the "obvious to try" rationale, which has often been rejected by the Court of Appeals for the Federal Circuit. The Supreme Court did not indicate that "obvious to try" is always an appropriate rationale for proving obviousness. On the contrary, the Court stated, "[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable

solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp . . . In that instance, the fact that a combination was obvious to try might show that it was obvious under § 103.” See KSR, at 1742. (Emphasis added.)

Additionally, the USPTO recently issued Examination Guidelines for Determining Obviousness Under 35 § U.S.C. 103 in View of the Supreme Court Decision in *KSR International Co. v. Teleflex Inc.* These guidelines discuss the “obvious to try” rationale, stating that in order for an Examiner to reject a claim based on this rationale, the following must be articulated:

- 1) A finding that at the time of the invention, there had been a recognized problem or need in the art, which may include a design need or market pressure to solve a problem;
- 2) A finding that there had been a finite number of identified, predictable potential solutions to the recognized need or problem;
- 3) A finding that one of ordinary skill in the art could have pursued the known potential solutions with a reasonable expectation of success; and
- 4) Whatever additional findings based on the *Graham* factors may be necessary, in view of the facts of the case under consideration, to explain a conclusion of obviousness.

Relevance of the KSR Decision to Current Application

As discussed above, the Chu, Nanbu et al. and Uenoyama et al. references teach **many surfactants**. The Nanbu et al. reference discloses that the surfactants indicated therein have no limitation in kind, and may be an ionic surfactant, an ampholytic surfactant, or a non-ionic surfactant. Nanbu et al. place no criticality on the particular surfactant to be employed. This broad and generic disclosure includes most of the surfactants existing in the world. Accordingly, the reference teaches surfactants which have the effect of Applicants’ invention together with surfactants which do not have the effect of Applicants’ invention, with no distinction.

Further, while both the Nanbu et al. and Uenoyama et al. references relate to a method for measuring urinary trypsin inhibitor (UTI), and both references employ a proteolytic enzyme, a low-water solubility substrate, an organic solvent or the like, it is apparent from the construction and the field of the Nanbu et al. and Uenoyama et al. references, that the teachings are very different from that of Applicants' presently claimed invention. That is, in the technical field of the Nanbu et al. and Uenoyama et al. references, many surfactants which do not have the effect of Applicants' invention are taught together in the same column, with no distinction, with surfactants which do have the effect of Applicants' presently claimed invention.

There are many different kinds of surfactants in the world, and the total number of surfactants may amount to several thousands. In addition, the surfactants have, in view of their chemical natures, various characteristics such as detergent property, foaming property, emulsifiability, permeability, solubilization, dispersibility, flexibility, dye-retarding property, spreading property, antiseptic property, antistatic property, and the like.

As discussed above regarding KSR, the Supreme Court has indicated that the "obvious to try" rationale is appropriate only where there is a finite number of identified, predictable solutions with a reasonable expectation of success. **Given the very large number of known surfactants, it cannot be said that picking and choosing from among this large number would be considered a finite number of identified, predictable solutions**. Accordingly, under the Supreme Court's discussion regarding the "obvious to try" rationale, the Examiner's position is untenable and should be withdrawn.

Inappropriate Hindsight Rationale

Additionally, Applicants respectfully submit that one of ordinary skill in the art would not have chosen a surfactant which is solidified when dried and which has a sugar in its hydrophilic part from the broad teachings of the cited references, without the benefit of Applicants' disclosure. As also stated by the Supreme Court in KSR, "the factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning." (See KSR, referring to Graham

v. John Deere Co. of Kansas City, 86 S. Ct. 684, which warned against a “temptation to read into the prior art the teachings of the invention in issue” and instructing courts to “guard against slipping into the use of hindsight”. Accordingly, the Examiner’s rejection is untenable on this basis as well.

Additional Comments

According to Applicants’ presently claimed invention, by using a surfactant which has sugar in a hydrophilic part which is able to become solid when dried, it is possible to 1) reduce influences on the specific protein which is immobilized to the reaction layer, and 2) to minimize denaturation or deactivation. Thus, the presently claimed invention 3) provides an immuno-chromatography device which achieves the enhancement of the preservation stability of the chromatography specimen, 4) the lengthening of the quality preservation period and 5) the relaxation of the maintenance condition.

The immuno-chromatography device is widely applied with a clinical inspection field as its center. The measurements thereof are especially important in this clinical inspection field, because the measurement result may influence human lives. On the other hand, the immuno-chromatography device is also a device by which an inspection can be carried out in a short time with an easy measurement operation by a user who is poor in specialty techniques, such as experimental techniques, inspection techniques, or in knowledge, and thus this device is widely prevalent in the POCT (Point-of-Care-Testing) field. There are very important technical issues for such inspection devices which are developed in this type of market, such as ensuring preservation stability for retaining performance for a longer period of time, easing preservation environment (for example, from a chilled storage to a room temperature storage) in the process of a manufactured product being shipped and distributed in the market, or being in the preservation period until the user actually uses the product.

The presently claimed invention cannot be easily realized by a person skilled in the art. Specifically, in a similar field, such as the Chu reference, the above-mentioned problem in the market should be supposed. Thus, if more than 30 kinds of surfactants are

taught, one skilled in the art should consider the characteristics of these surfactants, and suggest a surfactant such as that recited by Applicants, or which has the same characteristics as that recited by Applicants. However, this is not the case, as Chu does not even mention Applicants' recited surfactant. On the other hand, in the Nanbu et al. and Uenoyama et al. references, where the field is entirely different from Applicants' presently claimed invention, a dissolubility of a hardly-soluble substrate can be improved by using the surfactant in a process of diluting a hardly-soluble substrate, and the sensitivity can be improved by increasing the substrate addition amount. In the fields and constructions of the Nanbu et al. and Uenoyama et al. references, the surfactants which do not have the effect of Applicants' recited surfactants, and the surfactants which do have the effect of Applicants' recited surfactants, are taught in the same column with no distinction, as materials having the same characteristics. This is clearly contrary to Applicants' presently claimed invention.

The Examiner has stated several times that Applicants' arguments do not relate to the combination of references. However, Applicants respectfully assert that the arguments clearly relate to the combination of references. Specifically, Applicants argue that it would be illogical to one skilled in the art to combine the references in the manner suggested by the Examiner. The primary reference (Chu) has similar construction to Applicants' presently claimed invention, but does not teach or suggest the recited surfactant. The secondary references (Nanbu et al. and Uenoyama et al.) teach many surfactants, including those which do have the effect of Applicants' recited surfactant and those which do not. Neither of the secondary references teach or suggest any distinction among the disclosed surfactants. In view of the fact that the kind and nature of each particular surfactant is diverse, Applicants assert that one of ordinary skill in the art would not have achieved Applicants' claimed invention from the combinations of references asserted by the Examiner.

Thus, the subject matter of Applicants' claims 5, 12, 27, 31, 41, 45, 53 and 60 is clearly patentable over the cited combination of references.

Rejection under 35 U.S.C. § 103(a) over Chu in view of Nanbu et al. or Uenoyama et al.
and further in view of Iwata et al. (U.S. 5,912,139)

The rejection of claim 49 under 35 U.S.C. § 103(a) as being unpatentable over Chu in view of Nanbu et al. or Uenoyama et al. and further in view of Iwata et al. (U.S. 5,912,139) is respectfully traversed.

The comments set forth above are equally applicable to this rejection. Since claim 49 is directly dependent on claim 12, the subject matter of claim 49 is patentable over Chu in view of Nanbu et al. or Uenoyama et al. for the same reasons that the subject matter of claim 12 is patentable over this combination of references. The teachings of Iwata et al. do not remedy the deficiencies of these references.

Thus, the subject matter of claim 49 is patentable over the teachings of Chu in view of Nanbu et al. or Uenoyama et al. and further in view of Iwata et al.

Conclusion

Therefore, in view of the above remarks, it is submitted that each of the grounds of rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

If, after reviewing this Response, the Examiner feels there are any issues remaining which must be resolved before the application can be passed to issue, the Examiner is respectfully requested to contact the undersigned by telephone in order to resolve such issues.

Respectfully submitted,

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